From:	Brent Ranalli
To:	Hernandez-Quinones, Samuel
Cc:	Jonathan.Koplos@cadmusgroup.com
Subject:	Memo - Drinking Water PAGs Based on Doses to Critical Organs - 4-30-15docx.docx
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Hi Sam,

Here is the memo with an approach for using critical organs as the basis for PAGs, with a discussion of pros and cons and a list of critical organs and dose and risk coefficients for the list of 50+ isotopes you provided.

All best,

Brent

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Discussion of Drinking Water PAGs Based on Doses to Critical Organs as Opposed to Effective Whole Body Dose Commitment

SC&A and The Cadmus Group

April 30, 2015

EPA's Office of Water is currently researching strategies for developing Protective Action Guides (PAGs) and associated Derived Response Levels (DRLs) for drinking water. Specifically, the Agency recognizes a short-term emergency drinking water guide may be useful for public health protection in light of the Fukushima nuclear power plant accident, which impacted some Japanese drinking water supplies. One of the issues under consideration by the EPA is whether PAGs and DRLs for drinking water should take into consideration the critical organ. For example, the EPA is currently considering establishing separate drinking water PAGs and associated DRLs for children and adults using dose conversion factors and daily drinking water rates as set forth in Federal Guidance Report No. 13 (FRG-13). Consideration is being given to establishing PAGs of 500 mrem and 100 mrem effective dose commitment for adults and children, respectively. However, it is recognized that certain radionuclides concentrate in specific organs, such as Sr-90 in bone and I-131 in the thyroid gland. The Food and Drug Administration recognizes the importance of radionuclides that seek out and concentrate in specific organs and provides guidance with respect to these issues as applied to the PAGs for food.[1] In summary the food PAGs are as follows:

> *The PAGs are 5 mSv (0.5 rem) for committed effective dose equivalent or 50 mSv (5 rem) committed dose equivalent to an individual tissue or organ, whichever is more limiting.*

This approach takes into consideration that the doses to some organs from the ingestion of some radionuclides could be considerably higher than the effective whole body dose.

Should the Office of Water consider establishing selected organ specific PAGs for drinking water, one defensible strategy that can be used to derive organ-specific PAGs would involve the following steps:

1. Establish benchmark values for the lifetime risk of cancer associated with 100 mrem for children and 500 mrem for adults.

[1] Food and Drug Administration (FDA). 1998. Accidental Radioactive Contamination of Human Food and Animal Feeds: Recommendations for State and Local Agencies. Radiation Programs Branch, Division of Mammography Quality and Radiation Programs, Office of Health and Industry Programs. August 13, 1998

2. Determine the doses to particular organs that would be associated with the equivalent risk. These would then represent the PAGs for particular organs.
3. Identify the radionuclides that might require organ specific PAGs because they tend to concentrate in specific organs.
4. Calculate DRLs for those radionuclides for children and adults.

This memo presents two example of how this might be done, and discusses the pros and cons of the approach.

1.0 Cancer Risk Coefficients

Using the EPA Revised Blue Book[2], the cancer incidence coefficient for uniform whole body dose to low level radiation to a reference stationary population distribution (defined the 2000 U.S. vital statistics) is about 0.0001 risk per rem effective dose. A more precise estimate of the risk coefficient for a reference population, in units of risk per Gray (Gy^{-1}), is provided in Table 1.[3]

Table 1. Cancer Risks for a Reference U.S. Population (Gy^{-1})

	Whole Population		Females	Males
	mean	90% CI	mean	mean
Morbidity	0.116	0.056-0.213	0.135	0.0955
Mortality	0.058	0.028-0.10	0.0689	0.0469

Source: EPA Blue Book, pp. 2-3

The implications are that if 10,000 people in a standard U.S. population experienced a uniform whole body low linear energy transfer exposure of 500 mrem, 5 people would be expected to develop a radiogenic cancer over the course of the population's life expectancy.

The EPA revised Blue Book explains that *radiogenic risks for childhood exposures are of special interest. Doses received from ingestion or inhalation are often larger for children than adults, and the risks per unit dose are substantially larger for exposures during childhood (here defined as the time period ending at the 15th birthday) than from exposures later in life.* Table 2 presents the cancer risk coefficients for children, which appear to be about twice those for adults.

[2] EPA Radiogenic Cancer Risk Models and Projections for the United States, EPA 402-R-11-001, U.S. Environmental protection Agency, Office of Radiation and Indoor Air. April 2011

[3] The conversion from risk per Gray (as found in the revised Blue Book) to risk per rem is performed on the assumption that 1 Gray = 100 rem. This equivalence holds for beta and gamma radiation. The case of alpha emitters is more complicated. For simplicity's sake, for the purpose of this memo, simple equivalence is assumed.

Table 2. Cancer Risks for Children (under 15 years, (Gy^{-1})

	Females	90% CI	Males	90% CI
Morbidity	0.33	0.12-0.55	0.2	0.077-0.36
Mortality	0.15	--	0.085	--

Source: EPA Blue Book, p. 3

The revised Blue Book explains that there is generally much more uncertainty in the estimated risks from childhood exposures than in the risks for the entire population. A-bomb survivors who were children at the time of the bombings (ATB) still have substantial years of life remaining in which cancers are to be expressed. Further follow-up will provide more statistical precision and greater clarity as to how these risks vary many decades after the exposure. The implications of these risk coefficients are that if 10,000 children in a standard U.S. population experienced a uniform whole body low line[illegible]ergy transfer exposure of 100 mrem, between 2 and 3.3 children would be expect[illegible]to dev[illegible]op a radiogenic cancer over the course of the population's life expectancy. Of c[illegible]se the unc[illegible]ainties are high, the values differ somewhat between males and females, and, amo[illegible] children[illegible]he ri[illegible] would be higher for younger children.

2.0 Adult Doses to Critical O[illegible]s that [illegible]ould Be Associated with a Lifetime Morbidity Risk of 5E-4

For simplicity, let us assume a lifetime [illegible]sk coeffi[illegible]nt of 0.001 total cancer risk per rem uniform whole body exposure for adults. Hence, [illegible]for a[illegible]ults of 500 mrem effective dose would be associated with an individual lifetime excess total [illegible]ncer ri[illegible]of about 5E-4. Let us next assume that we would like to determine the I-131 and Sr-[illegible] exp[illegible]re to t[illegible] limiting organs that would be equivalent to a lifetime cancer risk of 5E-4. In th[illegible]ollow[illegible]g secti[illegible]s, we explore how one would derive PAGs and associated DRLs using the critical organ appro[illegible]h.

2.1 I-131

As can be seen in Appendix A, the limiting adult dose conversion factor for I-131 is 4.32E-7 Sv/Bq for the thyroid, and the limiting adult risk coefficient is 4.39E-10 risk/Bq for thyroid cancer. The organ specific PAG for thyroid cancer associated with the ingestion of I-131 in water would be derived as follows:

Thyroid Cancer: 4.39E-10 risk/Bq ÷ 4.32E-7 Sv/Bq = 1.02E-3 risk per Sv

The dose to the thyroid gland that would result in a lifetime risk of cancer of 5E-4 is as follows:

Thyroid Cancer: 5E-4 risk ÷ 1.02E-3 risk/Sv = 0.490 Sv or 49,000 mrem

Hence, if one were interested in establishing an I-131 PAG based on critical organ, with the same lifetime risk of cancer to that organ as an effective whole body dose of 500 mrem, the PAG would be 49,000 mrem to the thyroid; i.e., 98 times higher than the whole body dose.

The DRL is calculated as follows:

$$DRL_{organ} = PAG_{organ} / [\text{Ingestion rate} \times 365 \text{ days} \times DCF_{organ}]$$

For easy comparison with the whole-body DRL in the draft PAG chapter, we apply the same drinking water ingestion rate that is used there: 1.643 L/day for 50 year old males.

Thyroid Cancer: DRL = 0.490 Sv / [1.643 L/d x 365 d x 4.32E-7 Sv/Bq] = 1,891 Bq/L

This DRL for thyroid cancer is equivalent to 51,100pCi/L, which is less protective than the parallel whole-body DRL of 10,384 pCi/L.

2.2 Sr-90

In Appendix A, we see that the limiting adult dose coefficient is 4.09E-7 Sv/Bq for bone surface and the limiting risk coefficient for the ingestion of Sr-90 is 9.48E-10 lifetime risk of leukemia (which is primarily due to exposure of red bone marrow) per Bq of Sr-90 ingested. In order to determine which organ should be considered the "critical" organ, we calculate results for both. From the FGR-13 software version 2.0.13 (the source of the summary information in Appendix A) we find that the dose coefficient for red bone marrow is 1.79E-7 Sv/Bq and the risk coefficient for bone cancer is 3.98E-11 risk/Bq. Using both approaches, we obtain the following:

Leukemia: 9.48E-10 risk/Bq ÷ 1.79E-7 Sv/Bq = 5.30E-3 risk per Sv

Bone Cancer: 3.98E-11 risk/Bq ÷ 4.09E-7 Sv/Bq = 9.73E-5 risk per Sv

Clearly, the risk per Sv is much higher for exposure to the red bone marrow, even though the dose coefficient for bone surface is higher than for bone marrow. Hence, in this case, it would seem that a critical organ-based PAG for Sr-90 ingestion would be based on exposure to red bone marrow.

Organ-specific PAGs associated with a lifetime risk of cancer of 5E-4 would be calculated as follows:

Leukemia: 5E-4 risk ÷ 5.30E-3 risk/Sv = 9.43E-2 Sv or 9,430 mrem

Bone Cancer: 5E-4 risk ÷ 9.73E-5 risk/Sv = 5.14 Sv or 514,000 mrem

Hence, if one were interested in establishing a Sr-90 PAG based on critical organ, one would use red bone marrow, which is associated with the same lifetime risk of cancer as the effective whole body dose 500 mrem, and the PAG would be 9,430 mrem to red bone marrow, instead of 500 mrem effective whole body dose; i.e., about 19 times higher.

DRLs would be calculated as follows (using the 20-year-old male drinking water ingestion rate of 1.137 L/day, as per the draft PAG chapter):

Leukemia: DRL = 9.43E-2 Sv / [1.137 L/d x 365 d x 1.79E-7 Sv/Bq] = 1,270 Bq/L

Bone Cancer: DRL = 5.14 Sv / [1.137 L/d x 365 d x 4.09E-7 Sv/Bq] = 30,300 Bq/L

These DRLs are equivalent to 34,300 pCi/L (leukemia) and 818,000 pCi/L (bone cancer). The leukemia DRL is about twenty-four times more protective than the bone cancer DRL, but still about five times less protective than the whole-body DRL of 6,743 pCi/L in the draft PAG chapter.

Note that the DRL of 6,743 pCi/L in the draft PAG chapter is not for Sr-90 alone, but for Sr-90 and its decay product Y-90 together. Sr-90 normally occurs in environmental media accompanied by Y-90 in a stable ratio. There are two ways in which the risk posed by Y-90 could be taken into account. One is to calculate a separate PAG for Y-90. In this case, as in the case of Sr-90, we find that the critical organs for dose and risk do not match up. The limiting DCF for Y-90 is 3.15E-08 for the wall of the lower large intestine, while the limiting risk coefficient for Y-90 is 1.08E-10 risk of colon cancer. Here we encounter an additional complication: the menu of options for DCF does not include the colon as a target organ, and the menu of options for risk coefficient does not include cancer of the large intestine. So there is no straightforward way to determine whether a PAG for the colon or the large intestine is more limiting (or indeed to derive an organ-specific PAG at all for either organ).

Another way to handle the Y-90 that is expected to co-occur with Sr-90 in water is to calculate a single PAG by summing their respective dose and risk coefficients for a single selected target organ (e.g., for bone cancer or leukemia). As it happens, the bone surface dose coefficient for Y-90 and the leukemia risk coefficient for Y-90 are so minuscule that they add nothing (when taken to three decimal places) to the total dose and risk of combined Sr-90 and Y-90. Thus the PAG for combined Sr-90 and Y-90 is identical to the PAG for Sr-90, and the contribution of environmental Y-90 to public health risk becomes invisible.

3.0 Discussion

The critical-organ-specific approach enables policy-makers to focus on risks to particular organs. However, there are several drawbacks and difficulties associated with this approach. One problem with an organ-based PAG is that while a radionuclide may preferentially dose an organ, it does not only dose that one organ. All of the other organs of the body receive a dose as well. As seen in the examples above, the I-131 DRL based on risk to the thyroid is less protective than the DRL based on equivalent risk to the whole body, and the Sr-90 (or Sr-90/Y-90) DRL based on risk of leukemia is less protective than the DRL based on equivalent risk to the whole body. In either case, if the organ-specific PAG is used, the total risk to that individual would exceed the lifetime limit.[4] This problem could potentially be addressed by adjusting the allowable organ

[4] For instance, in order to receive a dose of 0.490 Sv of I-131 to the thyroid gland, an individual would need to ingest 1.13E+6 Bq of I 131 (i.e., 0.490 Sv ÷ 4.32E-7 Sv/Bq = 1.13E+6 Bq). In addition to giving a dose to the

specific lifetime risk limit downward, so that an individual's total risk would not exceed 5E-4. Options for such adjustment could be discussed.

Regardless of the risk threshold chosen as the basis for an organ-specific PAG, establishing risk-based PAGs to critical organs presents technical challenges. One is that it is not always a straightforward matter to select the target organ. In the case of I-131, the same organ (thyroid) was associated with the highest risk coefficient and the highest dose coefficient. In the case of Sr-90, on the other hand, the highest risk coefficient belonged to leukemia (due to radiation to bone marrow) and the highest dose coefficient belonged to the bone surface (associated with risk of bone cancer). PAGs for both organs needed to be calculated to determine which organ was most limiting. In the case of Y-90, the critical organs for dose and risk were not only mismatched, but the authoritative look-up tables did not provide both dose and risk values, and so did not permit calculation of PAGs for these organs. In Appendix A, it can be seen that many of the radionuclides of interest, like Sr-90, have mismatched critical organs, and a fair number of these radionuclides, like Y-90, have critical organs (e.g., upper large intestine, lower large intestine, colon) that appear in only dose or risk look-up tables but not both. (A complete list of organs from the two sets of look-up tables, showing the extent of compatibility between the tables, appears in Appendix B.)

Another technical challenge, as we have seen in the case of Sr-90 and Y-90, is that PAGs for multiple isotopes cannot be summed in a straightforward manner if the critical organs are different. In the case of parent and daughter radionuclides that are expected to occur together in the environment like Sr-90 and Y-90, normal practice is to combine their dose coefficients and risk coefficients and treat them like one chemical. As we have seen, use of the limiting Sr-90 organ for combined Sr-90/Y-90 results in Y-90 contributing nothing to the resulting PAG and DRL.

All factors taken into consideration, it appears that PAGs based on committed effective whole body dose, as compared to critical organ committed equivalent, are more protective, and the DRLs can be derived in a more straightforward manner.

thyroid, the ingested I 131 would result in a whole body dose. The FGR-13 effective whole body dose equivalent for ingestion of I 131 is 2.18E-8 Sv/Bq , so the whole body dose would be 0.025 Sv, or 2,500 mrem—about five timeswhat the whole-body-based PAG would allow.

Appendix A

Comparison of Dose Conversion Factors and Risk Coefficients

1	2	3	4	5	6	7
Isotope	Dose Conversion Factor (DCF) for Adults (Sv per Bq ingested in drinking water)			Risk Coefficient for Adults Age 25-70 (risk per Bq ingested in drinking water)		
	Whole Body DCF	Critical Organ (highest organ-specific DCF)	Critical Organ DCF	Whole Body Risk Coefficient	Critical Organ (highest organ risk coefficient)	Critical Organ Risk Coefficient
Sr-90/Y-90[1]	3.04E-08	Bone Surface	4.09E-07	1.19E-09	Leukemia (Trabecular Bone)	9.48E-10
Cs-137	1.36E-08	LLI Wall	1.67E-08	6.02E-10	Residual	1.27E-10
I-131	2.18E-08	Thyroid	4.32E-07	4.47E-10	Thyroid	4.39E-10
Ba-140	2.60E-09	LLI Wall	2.[illegible]E-07	1.04E-10	Colon	8.67E-11
Ba-141	6.99E-11	Stomach Wall	3.04E-10	1.79E-12	Colon	8.81E-13
Ba-142	3.53E-11	Stomach Wall	2.03E-10	1.78E-13	Stomach	4.21E-13
Ce-141	7.11E-10	LLI Wall	8.6[illegible]E-09	2.8[illegible]E-11	Colon	2.76E-11
Ce-143	1.12E-09	LLI Wall	1.16E-08	4.44E-11	Colon	4.21E-11
Ce-144	5.23E-09	LLI Wall	6.66E-08	2.16E-10	Colon	2.10E-10
Co-58	7.49E-10	LLI Wall	3.99E-09	2.65E-11	Colon	1.43E-11
Co-58m	2.41E-11	LLI Wall	1.67E-10	9.1[illegible]E-13	Colon	7.93E-13
Cs-134	1.92E-08	LLI Wall	2.26E-08	8.51E-10	Residual	1.86E-10
Cs-134m	2.01E-11	Stomach Wall	1.15E-10	5.45E-13	Stomach	2.39E-13
Cs-137	1.36E-08	LLI Wall	1.67E-08	6.02E-10	Residual	1.27E-10
Cs-138	9.19E-11	Stomach Wall	7.04E-10	1.91E-12	Stomach	1.46E-12
I-131	2.18E-08	Thyroid	4.32E-07	4.47E-10	Thyroid	4.39E-10
I-133	4.28E-09	Thyroid	8.23E-08	1.35E-10	Thyroid	1.26E-10
I-134	1.08E-10	Stomach Wall	5.51E-10	3.02E-12	Stomach	1.14E-12

1	2	3	4	5	6	7
Isotope	Dose Conversion Factor (DCF) for Adults (Sv per Bq ingested in drinking water)			Risk Coefficient for Adults Age 25-70 (risk per Bq ingested in drinking water)		
	Whole Body DCF	Critical Organ (highest organ-specific DCF)	Critical Organ DCF	Whole Body Risk Coefficient	Critical Organ (highest organ risk coefficient)	Critical Organ Risk Coefficient
I-135	9.35E-10	Thyroid	1.60E-08	3.08E-11	Thyroid	2.44E-11
La-141	3.58E-10	ULI Wall	2.49E-09	1.22E-11	Colon	1.02E-11
La-142	1.82E-10	Stomach Wall	8.50E-10	4.95E-12	Colon	2.41E-12
Mn-54	7.22E-10	LLI Wall	2.44E-09	2.68E-11	Colon	9.49E-12
Mn-56	2.56E-10	ULI Wall	1.36E-09	7.79E-12	Colon	5.06E-12
Mo-99	6.05E-10	Kidneys	3.10E-09	2.41E-11	Liver	4.62E-12
Mo-101	4.15E-11	Stomach Wall	2.25E-10	8.83E-13	Stomach	6.76E-13
Nb-95	5.88E-10	LLI Wall	4.04E-09	2.01E-11	Colon	1.41E-11
Rb-89	4.68E-11	Stomach Wall	3.63E-10	9.58E-13	Stomach	7.55E-13
Ru-103	7.34E-10	LLI Wall	5.01E-09	2.80E-11	Colon	2.18E-11
Ru-106	7.01E-09	LLI Wall	7.78E-08	2.92E-10	Colon	2.30E-10
Sb-128[2]	7.63E-10	ULI Wall	3.95E-09	2.65E-11	Colon	1.92E-11
Sb-129	4.23E-10	ULI Wall	2.82E-09	1.51E-11	Colon	1.22E-11
Sb-130	9.19E-11	Stomach Wall	5.74E-10	2.19E-12	Stomach	1.19E-12
Sb-131	1.03E-10	Thyroid	7.07E-10	2.58E-12	Thyroid	1.08E-12
Sn-128	1.55E-10	Stomach Wall	8.37E-10	3.90E-12	Stomach	1.74E-12
Sr-89	2.57E-09	LLI Wall	2.22E-08	1.36E-10	Colon	7.06E-11
Sr-90	2.77E-08	Bone Surface	4.09E-07	1.08E-09	Leukemia (Trabecular Bone)	9.48E-10
Sr-91	6.50E-10	LLI Wall	3.97E-09	2.44E-11	Colon	1.94E-11
Sr-92	4.26E-10	ULI Wall	3.07E-09	1.64E-11	Colon	1.36E-11
Tc-101	1.88E-11	Stomach Wall	1.50E-10	3.52E-13	Stomach	3.11E-13
Tc-104	8.01E-11	Stomach Wall	6.21E-10	1.56E-12	Stomach	1.29E-12
Te-131	8.75E-11	Thyroid	8.91E-10	2.20E-12	Thyroid	1.36E-12
Te-131m	1.95E-09	Thyroid	1.85E-08	6.75E-11	Colon	3.00E-11

1	2	3	4	5	6	7
Isotope	Dose Conversion Factor (DCF) for Adults (Sv per Bq ingested in drinking water)			Risk Coefficient for Adults Age 25-70 (risk per Bq ingested in drinking water)		
	Whole Body DCF	Critical Organ (highest organ-specific DCF)	Critical Organ DCF	Whole Body Risk Coefficient	Critical Organ (highest organ risk coefficient)	Critical Organ Risk Coefficient
Te-132	3.81E-09	Thyroid	3.11E-08	1.43E-10	Colon	6.36E-11
Te-133	7.24E-11	Thyroid	8.14E-10	1.91E-12	Thyroid	1.24E-12
Te-133m	2.83E-10	Thyroid	3.22E-09	8.18E-12	Thyroid	4.91E-12
Te-134	1.08E-10	Thyroid	5.26E-10	3.24E-12	Stomach	9.30E-13
Y-91	2.37E-09	LLI Wall	3.03E-08	9.74E-11	Colon	9.59E-11
Y-92	4.95E-10	ULI Wall	3.34E-09	1.64E-11	Colon	1.33E-11
Y-93	1.15E-09	LLI Wall	7.75E-09	4.46E-11	Colon	4.18E-11
Y-94	8.15E-11	Stomach Wall	6.42E-10	1.54E-12	Stomach	1.33E-12
Y-95	4.63E-11	Stomach Wall	3.75E-10	8.43E-13	Stomach	7.80E-13
Zr-95	9.61E-10	LLI Wall	3.53E-09	3.53E-11	Colon	2.60E-11
Zr-97	2.07E-09	LLI Wall	1.28E-08	8.03E-11	Colon	7.37E-11
Sr-90	2.77E-08	Bone Surface	4.09E-07	1.38E-09	Leukemia (Trabecular Bone)	9.48E-10
Y-90	2.69E-09	LLI Wall	3.15E-08	1.10E-10	Colon	1.08E-10

Source: FGR-13 software, version 2.1.13. This is the same version used in development of the draft PAG chapter. For an explanation of abbreviations, see Appendix B.

[1] For combined Sr-90 and Y-90, the contribution of both Sr-90 and Y-90 to the critical organ of Sr-90 is summed. The contribution of Y-90 turns out to be negligible.

[2] The FGR-13 software has two listings for Sb-128, with half lives of 10.4 minutes and 9.01 hours. The listing with the longer half-life was selected for the purpose of this table.

Appendix B

Target Organs Listed in Dose and Risk Lookup Tables from FGR-13

Organs In Dose Tables	Organs (Cancer Types) In Risk Tables
Adrenals	
B_Surface (bone surface)	Bone
Brain	
Breast	Breast
St_Wall (stomach wall)	Stomach
SI_Wall (small intestine wall)	
ULI_Wall (upper large intestine wall)	
LLI_Wall (lower large intestine wall)	
Kidneys	Kidney
Liver	Liver
ET-Region (extrathoracic region)	
Lung	Lung
Muscle	
Ovaries	Ovary
Pancreas	
R_Marrow (red bone marrow)	Leukemia (trabecular bone)
Skin	Skin
Spleen	
Testes	
Thymus	
Thyroid	Thyroid
Uterus	
UB_Wall (urinary bladder wall)	Bladder
	Colon
	Esophagus
	Residual

Source: FGR-13 software, version 2.1.13